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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/581,651	10/10/2000	Seth Lawrence Schor	002.00120	4652

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EXAMINER

RAWLINGS, STEPHEN L

ART UNIT	PAPER NUMBER
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1643

DATE MAILED: 01/23/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b> 09/581,651	<b>Applicant(s)</b> SCHOR ET AL	
	<b>Examiner</b> Stephen L. Rawlings, Ph.D.	<b>Art Unit</b> 1643	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 6/8/05, 8/18/05, and 11/10/05.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1,4,5,7-9,29,60 and 61 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☒ Claim(s) 29 is/are allowed.
- 6) ☒ Claim(s) 1,4,5,7-9,60 and 61 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 6/8/05 is/are: a) ☐ accepted or b) ☒ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input checked="" type="checkbox"/> Other: <u>See Continuation Sheet</u> .           |

Continuation of Attachment(s) 6). Other: U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 2), pages 1-5.

### **DETAILED ACTION**

1. The amendment filed November 10, 2005, is acknowledged and has been entered. Claims 2, 3, 10, 11, 26-42, 44, 47-51, 53, 56, and 58 have been canceled. Claims 1, 4, 5, 8, 9, and 29 have been amended. Claims 60 and 61 have been added.
2. The amendment filed August 18, 2005, is acknowledged and has been entered. Claims 6, 12, 13, 27, 57, and 59 have been canceled. Claims 1, 2, 4, 5, 8-11, 29, 36-38, 40-42, 47, 51, 56, and 58 have been amended.
3. The amendment filed June 8, 2005, is acknowledged and has been entered in part.
4. Claims 1, 4, 5, 7-9, 29, 60, and 61 are currently under prosecution.
5. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

### ***Election/Restrictions***

6. The requirement to elect a species of the invention of Group I set forth in section 8 of the Office action mailed May 3, 2002, has been withdrawn.

### ***Drawings***

7. Receipt of the replacement drawings filed June 8, 2005, is acknowledged. The drawing depicting Figure 3 is acceptable; however, the drawing depicting Figure 2 is not because in both instances "SEQ ID NO." is misspelled as "SEQ IS NO.".

### ***Response to Amendment***

8. At page 4 of the amendment filed November 10, 2005, Applicant has stated, "the Examiner agreed that a polynucleotide whose sequence is SEQ ID NO:2 is patentable".

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Notably SEQ ID NO: 2 is an amino acid sequence, and contrary to any implication that a claim drawn to polypeptide comprising SEQ ID NO: 2 is patentable, it is not. During the interview the Examiner explained the reasons why such a claim is not patentable over the prior art of record, but noted that since the polynucleotide sequence of SEQ ID NO: 3 is free of the prior art, the claims could be amended to overcome the rejections that are currently of record over the prior art. As explained in the Interview Summary mailed November 9, 2005, the Examiner proposed entry of an examiner's amendment, which would place this application in condition for allowance, but Applicant's representatives opted not to authorize its entry in favor of filing a supplemental amendment.

#### ***Grounds of Objection and Rejection Withdrawn***

9. Without acquiescing to Applicant's arguments, the rejections of claims under 35 U.S.C. §§ 102 or 103, as being anticipated by Grey et al., as evidenced by Schor et al., or obvious Grey et al., as evidenced by Schor et al., in view of Bendig, for the reasons set forth in sections 25 and 29 of the preceding Office action have been withdrawn in favor of the new grounds of rejection set forth below.

Otherwise, unless specifically reiterated below, Applicant's amendment and/or arguments filed June 8, 2005, August 18, 2005, and/or November 10, 2005, have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed December 7, 2004.

#### ***Grounds of Objection and Rejection Maintained***

##### ***Drawings***

10. The objection to the drawing sheet setting forth Figure 2 (Part 2), because "SEQ ID NO." is misspelled as "SEQ IS NO." in both instances, is maintained. As noted above, although a replacement sheet was filed June 8, 2005, this issue has not been resolved. Appropriate correction is required.

**Specification**

11. The objection to the specification, because the use of improperly demarcated trademarks, is maintained. Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner that might adversely affect their validity as trademarks. See MPEP § 608.01(v).

Although it appears Applicant has made a *bona fide* attempt to correct this issue, another example of an improperly demarcated trademark is found at page 47, line 19, of the substitute specification filed June 8, 2005, namely pBlueScript™.

Appropriate correction is required. Each letter of a trademark should be capitalized or otherwise the trademark should be demarcated with the appropriate symbol indicating its proprietary nature (e.g., ™, ®), and accompanied by generic terminology. Applicants may identify trademarks using the "Trademark" search engine under "USPTO Search Collections" on the Internet at <http://www.uspto.gov/web/menu/search.html>.

**Claim Rejections - 35 USC § 112**

12. The rejection of claims 9 and 61 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, is maintained.

Claims 9 and 61 are indefinite because the claims recite a limitation that the polypeptide has "the migration stimulating factor activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2". Although claims 9 and 61 depend directly or directly from claim 1, which defines the migration stimulation activity of a polypeptide having the amino acid sequence of SEQ ID NO: 2 as "[the] ability to stimulate adult skin fibroblast migration into collagen gel", claims 9 and 61 are not necessarily so limited, since claims 9 and 61 are only required to be processes comprising culturing a host cell comprising a polynucleotide according to claim 1. In other words, although the host cells cultured in the claimed processes comprise a polynucleotide according to claim 1, the recitation does not limit the method to a process for making a polypeptide having

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"[the] ability to stimulate adult skin fibroblast migration into collagen gel", because the polypeptide made according to the claimed process is not necessarily a polypeptide encoded by a polynucleotide according to claim 1. Furthermore, as explained in the preceding Office action, the specification does not clearly and particularly define what functional activity or activities constitute "the migration stimulating factor activity" of the polypeptide of SEQ ID NO: 2. Accordingly, the metes and bounds of the subject matter that Applicant regards as the invention cannot be ascertained with the requisite degree of particularity and clarity, so as to permit the skilled artisan to determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

13. The rejection of claims 1, 7, 8, 9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At pages 11 and 12 of the amendment filed June 8, 2005, and at pages 11 and 12 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

The claims are directed to nucleic acid molecules encoding a genus of structurally and functionally variable polypeptides. More specifically the claims are directed to nucleic acid molecules having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Moreover, the claims are not limited to nucleic acid molecules comprising the disclosed polynucleotide

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sequences that encode a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, but rather encompass nucleic acid molecules encoding variants of this polypeptide.

Although the members of the claimed genus of nucleic acid molecules necessarily comprise a polynucleotide sequence that is at least 90% homologous to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the members are not required to have any particular degree of identity to the disclosed polynucleotide sequence of SEQ ID NO: 3, which encodes the amino acid sequence of SEQ ID NO: 2. Accordingly, the claims are directed to a genus of nucleic acid molecules that vary substantially in structure.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, which elicits antibodies that recognize "migration stimulation factor", but not fibronectin, the polypeptides themselves are not required to have any degree of structural homology (i.e., similarity) or identity to the amino acid sequence of SEQ ID NO: 2. Accordingly, the claims are directed to a genus of nucleic acid molecules that vary substantially in structure and encode polypeptides, which although commonly having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and commonly having the ability to elicit antibodies that recognize "migration stimulation factor", but not fibronectin, vary substantially in structure.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, the members of the genus cannot be immediately envisioned, recognized or distinguished from other nucleic acid molecules encoding other proteins. The specification describes only one polypeptide encoded by the claimed genus of nucleic acid molecules, namely the polypeptide of SEQ ID NO: 2. Neither the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 (e.g., the nucleic acid molecule of SEQ ID NO: 3) nor the polypeptide itself are described in sufficient and detailed manner, so as to reasonably be considered



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representative of the genus, as a whole, since there is no disclosure of a particularly identifying (i.e., substantial) structural feature shared by at least most of the polypeptides encoded by the claimed nucleic acid molecules that correlates with the polypeptides' ability to stimulate adult skin fibroblasts migration into collagen gel, which is at least 30% of the same activity of a polypeptide comprising SEQ ID NO: 2.

Although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides that elicit antibodies that recognize "migration stimulation factor", but not fibronectin, the members of the genus cannot be immediately envisioned, recognized or distinguished from other nucleic acid molecules encoding other proteins. Again, the specification describes only one polypeptide encoded by the claimed genus of nucleic acid molecules, namely the polypeptide of SEQ ID NO: 2. Neither the nucleic acid molecules encoding the polypeptide of SEQ ID NO: 2 (e.g., the nucleic acid molecule of SEQ ID NO: 3) nor the polypeptide itself are not described in sufficient and detailed manner, so as to reasonably be considered representative of the genus, as a whole, since there is no disclosure of the presence of a shared, particularly identifying structural feature, which in this case is necessarily a common antigenic determinant (i.e., the epitope to which an antibody that recognizes the protein encoded by the claimed nucleic acid molecule, which is not presented by fibronectin), that correlates with their shared "migration stimulation factor activity". Moreover, the recitation of a limitation requiring the polypeptide encoded by the members of the claimed genus of nucleic acid molecules to elicit an antibody that binds specifically to "migration stimulation factor", but not fibronectin, would not reasonably convey to the skilled artisan that, as of the filing date sought, the Applicant had possession of the claimed invention, because the recitation does not provide a description of any uniquely defining or identifying feature that is common to at least a substantial number of members of the claimed genus, which would descriptively set the genus apart from just any polypeptide encoded by a nucleic acid molecule having the required similarity (i.e., at least 90% homology) to the reference amino acid sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2.

With particular regard to claims 9 and 61, the claims are directed to methods for making a polypeptide having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a cell comprising a polynucleotide according to claim 1, but the polypeptide produced by the claimed methods is not necessarily a polypeptide encoded by the polynucleotide according to claim 1. Thus, claims 9 and 61 are directed to methods for making structurally variant polypeptides encoded by any nucleic acid molecule of which said host cell is comprised, which commonly have at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2.

The Federal Circuit has decided that a patentee of a biotechnological invention cannot necessarily claim a genus after only describing a limited number of species because there may be unpredictability in the results obtained from species other than those specifically enumerated. See *Noelle v. Lederman*, 69 USPQ2d 1508 1514 (CA FC 2004) (citing *Enzo Biochem II*, 323 F.3d at 965; *Regents*, 119 F.3d at 1568).

Insofar as the claims are directed to structurally varying nucleic acid molecules encoding polypeptides that differ both structurally and functionally from the disclosed polypeptides comprising the amino acid sequence of SEQ ID NO: 2, the specification fails to describe the claimed invention with the requisite detail and particularity that is necessary to satisfy the written description requirement set forth under 35 U.S.C. 112, first paragraph. "[G]eneralized language may not suffice if it does not convey the detailed identity of an invention." *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004). In this instance, there is no language that adequately describes the genus of nucleic acid molecules. A description of what a material does, rather than of what it is, does not suffice to describe the claimed invention.

Even whilst the nucleic acid molecules encompassed by the claims encode polypeptides that have recognizable functions, it is again aptly noted that the Federal Circuit has decided that a generic statement that defines a genus of substances by *only* their functional activity, i.e., the ability stimulate adult skin fibroblasts migration into collagen gel, which is at least 30% of the same activity of a polypeptide comprising SEQ

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ID NO: 2, and to elicit an antibody that cross-reacts with the polypeptide of SEQ ID NO: 2 without binding fibronectin, does not provide an adequate written description of the genus. See *The Regents of the University of California v. Eli Lilly*, 43 USPQ2d 1398 (CAFC 1997). The Court indicated that while applicants are not required to disclose every species encompassed by a genus; the description of a genus is achieved by the recitation of a precise definition of a representative number of members of the genus, such as by reciting the structure, formula, chemical name, or physical properties of those members, rather than by merely reciting a wish for, or even a plan for obtaining a genus of molecules having a particular functional property. The recitation of a functional property alone, which must be shared by the members of the genus, is merely descriptive of what the members of genus must be capable of doing, not of the substance and structure of the members.

In addition, although the skilled artisan could potentially screen candidate nucleic acid molecules to identify those that encode polypeptides that are encompassed by the claims, which have those recognizable functions, it is duly noted that the written description provision of 35 U.S.C § 112 is severable from its enablement provision; and adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it.

The purpose of the "written description" requirement is broader than to merely explain how to "make and use"; the applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of *the invention*. The invention is, for purposes of the "written description" inquiry, *whatever is now claimed*.

*Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ2d 1111, 1117 (CAFC 1991). See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993); *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016 (CAFC 1991); *University of Rochester v. G.D. Searle Co.*, 69 USPQ2d 1886 1892 (CAFC 2004).

Finally, Applicant is again reminded that Guidelines for Examination of Patent Applications Under the 35 U.S.C. 112, paragraph 1, "Written Description" Requirement (66 FR 1099-1111, January 5, 2001) states, "[p]ossession may be shown in a variety of ways including description of an actual reduction to practice, or by showing the

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invention was 'ready for patenting' such as by disclosure of drawings or structural chemical formulas that show that the invention was complete, or by describing distinguishing identifying characteristics sufficient to show that the applicant was in possession of the claimed invention" (*Id.* at 1104). Because the claims encompass a genus of nucleic acid molecules encoding polypeptides, which vary both structurally and functionally, an adequate written description of the claimed invention must include sufficient description of at least a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics sufficient to show that Applicant was in possession of the claimed genus. In this instance, factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; Applicant has not shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete; and Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed.

Thus, while the disclosure might be considered to provide *ipsis verbis* support for the claimed invention, the Federal Circuit has explained that *in ipso verbis* support does not *per se* establish compliance with the written description requirement:

Even if a claim is supported by the specification, the language of the specification, to the extent possible, must describe the claimed invention so that one skilled in the art can recognize what is claimed. The appearance of mere indistinct words in a specification or a claim, even an original claim, does not necessarily satisfy that requirement. The disclosure must allow one skilled in the art to visualize or recognize the identity of the subject matter purportedly described. *Eli Lilly*, 119 F.3d at 1568, 43 USPQ2d at 1406.

*Regents of the University of California v. Eli Lilly & Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). See also: *University of Rochester v. G.D. Searle & Co.*, 69 USPQ2d 1886 1892 (CA FC 2004).

14. The rejection of claims 1, 7, 8, 9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using** an isolated, recombinant nucleic acid molecule encoding a polypeptide

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comprising the amino acid sequence of SEQ ID NO: 2, an isolated, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3 from the nucleotide at position 57 through the nucleotide at position 1982, a isolated replicable vector comprising any of said polynucleotide sequences, an isolated host cell comprising said vector, and a method for producing said polypeptide by a process comprising culturing said host cell and isolating said polypeptide, or any nucleic acid molecule taught by the prior art, **does not reasonably provide enablement for making and using** a nucleic acid molecule having a polynucleotide sequence that is at least 90% homologous to a recombinant polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which stimulates adult skin fibroblasts migration into collagen gel with at least 30% of the same activity of a polypeptide comprising SEQ ID NO: 2 and elicits an antibody that cross-reacts with the polypeptide of SEQ ID NO: 2 without binding fibronectin, a replicable vector comprising said polynucleotide sequence, an isolated host cell comprising said polynucleotide sequence, or a method for producing a polypeptide that stimulates adult skin fibroblasts migration into collagen gel with at least 30% of that activity of a polypeptide comprising SEQ ID NO: 2, said method comprising culturing a host cell comprising said polynucleotide sequence and isolating the polypeptide. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make/or the invention commensurate in scope with these claims.

At pages 11 and 12 of the amendment filed June 8, 2005, and at pages 11 and 12 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

MPEP § 2164.01 states:

The standard for determining whether the specification meets the enablement requirement was cast in the Supreme Court decision of *Mineral Separation v. Hyde*, 242 U.S. 261, 270 (1916) which postured the question: is the experimentation needed to

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practice the invention undue or unreasonable? That standard is still the one to be applied. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). Accordingly, even though the statute does not use the term "undue experimentation," it has been interpreted to require that the claimed invention be enabled so that any person skilled in the art can make and use the invention without undue experimentation. *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

There are many factors to be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue". These factors, which have been outlined in the Federal Circuit decision of *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988), include, but are not limited to, the nature of the invention, the state of the prior art, the relative skill of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, the breadth of the claims, and the quantity of experimentation which would be required in order to practice the invention as claimed. See also *Ex parte Forman*, 230 USPQ 546 (BPAI 1986).

As explained above in the rejection of claims under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, the claims are directed to nucleic acid molecules of considerable structural variability, which encode polypeptides that differ markedly, both in structure and function. As explained in the preceding Office action, the state of the art, the level of skill in the art, and the unpredictability in the art are such that absent guidance, direction, and exemplification that is more reasonably commensurate in scope with the scope of the claims, the skilled artisan, at the time the application was filed, could not without undue and/or unreasonable experimentation make and/or use the claimed invention. This position is supported by references cited in the preceding Office action, including Skolnick et al. (of record), Burgess et al. (of record), and Lazar et al. (of record).

The claims are directed to nucleic acid molecules that encode variants of the disclosed polypeptide of SEQ ID NO: 2, which have or retain at least 30% of the ability of the polypeptide of SEQ ID NO: 2 to stimulate adult skin fibroblasts to migrate into collagen gel, as measured using an assay described by Picardo et al. (of record).

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However, as explained previously, the specification fails to teach which amino acid residues of SEQ ID NO: 2 are critical to this particular function of the polypeptide of SEQ ID NO: 2. Moreover, the specification fails to teach by which other amino acids such critical residues can be replaced without loss of activity. Absent such necessary guidance and direction, because the skilled artisan cannot reliably and accurately predict the effects of amino acid substitutions, deletions, or insertions in the amino acid sequence of a given polypeptide, the disclosure would not be sufficient to have enabled the skilled artisan at the time the application was filed to make, and therefore use, the claimed invention.

Furthermore, there is no factual evidence of record that reasonably supports any assertion that the mere presence of a common antigenic determinant correlates with, or determines a common "migration stimulation factor activity" of any polypeptide encoded by nucleic acid molecules having sequences that are at least 90% homologous (i.e., similar to) a nucleic acid molecule encoding a polypeptide comprising SEQ ID NO: 2. Therefore, although the members of the claimed genus of nucleic acid molecules necessarily encode polypeptides that elicit antibodies that recognize "migration stimulation factor", but not fibronectin, it is submitted that the members of the genus cannot be distinguished from other nucleic acid molecules encoding other proteins simply by using the encoded polypeptide to elicit antibodies and then determining if the antibodies bind the polypeptide without binding fibronectin. As such, the requirement that the claimed nucleic acid molecules encode antigenically related polypeptides does not remedy the insufficiency of the guidance and direction that would otherwise, if present and sufficient, enable the skilled artisan to make the claimed nucleic acid molecules encoding variants of the polypeptide of SEQ ID NO: 2.

Echoing this fact, Takada et al. (*Mol. Endocrinol.* 2000; **14** (5): 733-740) teaches that the lack of predictability in the art remains, despite technological advances and a better understanding of the structure-function relationship; see entire document (e.g., the abstract). Takada et al. teaches their work illustrates that a single amino acid change may be sufficient to cause the acquisition of a new ligand binding specificity as well as to suppress recognition of a previous ligand, extending observations by others

who showed that changes in one or several amino acids can result in marked alterations in activity and function of nuclear receptors (page 738, column 1). Notably, Takada et al. teaches that the functional consequence of amino acid substitution may be rather subtle, since the variants of the receptors were still able to bind to the promoter of the reporter construct and activate transcription in the presence of some ligands but not others; see, e.g., page 739, Figure 5. Takada et al. teaches the difference in ligand binding specificity caused by the amino acid changes results in the variants having the activity of different member of the family of proteins; see, e.g., the abstract. Thus, Takada et al. discloses that seemingly subtle differences resulting from amino acid differences, such as changes in ligand binding specificity, may cause variants of a protein to have a function that differs markedly from that of the protein. Accordingly, depending upon the assay used to assess the activity of the proteins and its variants, the effects of amino acid sequence variation may not be immediately recognized or appreciated, since the variants may appear to function normally otherwise, but in actuality have substantially different functions.

Even more recently, Guo et al. (*Proc. Natl. Acad. Sci. USA*. 2004 Jun 22; **101** (25): 9205-9210) have calculated the probability that a random amino acid substitution, such as that which might occur naturally during aging or as a consequence of evolution or disease, will cause inactivation of a protein; see entire document (e.g., the abstract). Guo et al. reports this probability was found to be  $34\% \pm 6\%$  (abstract); that is, 34% of random mutations in the sequence of a protein are predicted to cause the inactivation of the protein. Guo et al. observed that various residues are differentially sensitive to substitutions, but the tolerance of the entire protein to random change can be defined by the probability that any given random amino acid substitution will inactivate the protein (i.e., the so-called "x factor") (page 9209, column 2). Not surprisingly, evolutionarily conserved residues showed low substitutability indices (abstract).

Thus, Lazar et al. (of record), for example, shows that even a single, conservative amino acid change can cause substantial changes in the activity of a protein, so it is evident that the skilled artisan cannot predict the functional consequences of amino acid substitutions and must determine those consequences



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empirically; and since Guo et al. (*supra*) shows that amino acid substitutions are remarkably likely to cause inactivation of the protein, it is even more apparent that the functional consequences of the amino acid differences must be ascertained before any given variant of a protein can be used in the same manner in which the protein having a known function is used.

In conclusion, upon careful consideration of the factors used to determine whether undue experimentation is required, in accordance with the Federal Circuit decision of *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988), there is a preponderance of factual evidence of record that indicates the disclosure would not be sufficient to have enabled the skilled artisan to use the claimed invention at the time the application was filed without undue and/or unreasonable experimentation.

***Claim Rejections - 35 USC § 102***

15. The rejection of claims 1, 7-9, 60, and 61 under 35 U.S.C. 102(b), as being anticipated by WO 94/16085 A2 (of record), is maintained.

At page 14 of the amendment filed June 8, 2005, and at page 14 of the amendment filed August 18, 2005, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but are not found persuasive for the following reasons:

Claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or alternatively to a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claim 7 is drawn to a replicable vector comprising a recombinant polynucleotide according to claim 1. Claims 8 and 60 are drawn to an isolated host cell comprising a recombinant polynucleotide according to claim 1, or a replicable vector according to claim 7, respectively. Claims 9 and 61 are drawn to methods for making a polypeptide having at least 30% of the "migration

stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a host cell comprising a polynucleotide according to claim 1, or a host cell according to claim 60, respectively.

"Homology" is defined, for example, by Merriam-Webster Online Dictionary, which is available on the Internet at <http://www.merriam-webster.com/>, as "similarity of nucleotide or amino-acid sequence in nucleic acids, peptides, or proteins" (copyright 2005 by Merriam-Webster, Incorporated). Homology or similarity of nucleic acid sequences may be evaluated by relatively subjective criterion, or it may be objectively measured using any of a wide variety of differing criterion.

Accordingly, the claims are not limited to nucleic acid molecules comprising a polynucleotide sequence that is at least 90% identical to any particular polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, such as the polynucleotide sequence of SEQ ID NO: 3. Rather the claims are directed to a genus of structurally varying nucleic acid molecules that are somehow determined to be 90% homologous (i.e., similar) to a polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2.

WO 94/16085 A2 (Irani) teaches an isolated, recombinant nucleic acid molecule comprising a polynucleotide that encodes a polypeptide that is 97.1% identical to amino acid sequence of SEQ ID NO: 2; see entire document (e.g., SEQ ID NO: 2). Irani teaches the polypeptide encoded by the disclosed nucleic acid molecule is produced by a process comprising culturing a host cell comprising a replicable vector comprising a polynucleotide sequence encoding the polypeptide and purifying the polypeptide; see, e.g., page 8, line 27, through page 15, line 12.

When compared to the polynucleotide sequence of SEQ ID NO: 3, which is the disclosed polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the polynucleotide sequence disclosed by the prior art (i.e., SEQ ID NO: 1) has a "best local similarity" of 97.1%; see the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 3), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Although Irani et al. does not expressly teach the polypeptide encoded by the disclosed nucleic acid molecule has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and elicits antibodies that recognize "migration stimulation factor" but not fibronectin, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polynucleotide, replicable vector, and host cell, or for examining and comparing Applicant's process with process of the prior art to establish that the claimed method for making a polypeptide and the methods of the prior art produce distinguishable products.

Given the fact that the nucleic acid molecule disclosed by the prior art encodes a polypeptide having an amino acid sequence that is 94.8% identical to amino acid sequence of SEQ ID NO: 2, the claimed products and processes are deemed the same as those disclosed by the prior art, absent a showing of any difference.

In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. *See In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

### ***New Grounds of Rejection***

#### ***Claim Rejections - 35 USC § 101***

16. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1, 4, and 5 are specifically drawn to "recombinant" polynucleotides, whereas claims 7 is drawn to a replicable vector comprising a polynucleotide as defined in claim 1.

The Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2005 by Merriam-Webster, Inc.), which is available on the Internet at <http://www.m-w.com/>, defines the term "recombinant" as "relating to or containing recombinant DNA".

Because claims 1, 4, 5, and 7 are drawn to recombinant polynucleotides and replicable vectors comprising such polynucleotides, *which are not necessarily isolated*, the claims are broadly but reasonably interpreted to encompass nucleic acid molecules and replicable vectors that are present in cells, which are not isolated but rather comprised *within* an organism, including a human. Support for this interpretation of the claims is found throughout the specification; for example, at page 44, lines 10 and 11, the specification, as originally filed, contemplates the use of gene therapy to administer to patients (i.e., humans) the claimed replicable vector comprising the claimed nucleic acid sequence encoding the disclosed polynucleotide. Host cells comprised within the patient are “transformed” or “transfected” with the recombinant nucleic acid molecules encoding the polypeptide, or replicable vectors (e.g., retroviral vectors) comprising the polynucleotide sequences of such nucleic acid molecules; see, e.g., page 12, line 23, through page 13, line 28. Accordingly, the claims encompass such recombinant nucleic acid molecules and replicable vectors, which are comprised within the cells of treated patients.

MPEP § 2105 [R-1] states:

If the broadest reasonable interpretation of the claimed invention as a whole encompasses a human being, then a rejection under 35 U.S.C. 101 must be made indicating that the claimed invention is directed to nonstatutory subject matter.

With further regard to claims 1, 4, and 5, it is aptly noted the Merriam-Webster's Online Dictionary, 10th Edition (copyright © 2005 by Merriam-Webster, Inc.) provides an alternative definition of the “recombinant”, namely “relating to or exhibiting genetic recombination”. Given this definition, it is not apparent that the claimed subject matter is distinguishable from a naturally occurring polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the messenger RNA (mRNA) molecule of which human cells are naturally comprised, which encodes the polypeptide of SEQ ID NO: 2. Accordingly, giving the claims the broadest, reasonable interpretation that is consistent with both the specification and that which the skilled artisan would have, the claims are drawn to non-statutory subject matter (i.e., a naturally occurring product).

Moreover, claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide, or alternatively to a polynucleotide, albeit not necessarily recombinant or isolated having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 (e.g., a sequence at least 90% homologous to SEQ ID NO: 3) and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin.

These issues can be remedied by amending claims 1, 4, 5, and 7 to recite the limitation "isolated" before "recombinant polynucleotide" or "replicable vector".

***Claim Rejections - 35 USC § 112***

17. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is drawn a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the migration stimulation factor activity of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claims 7-9, 60, and 61 depend from claim 1.

The claims are indefinite because claim 1 uses the term "migration stimulation factor" to define the polypeptide by which antibodies elicited by the claimed polypeptide are recognized without also recognizing fibronectin. The use of laboratory designations only to identify a particular polypeptide renders the claims indefinite because different laboratories may use the same laboratory designations to define completely distinct polypeptides. In the absence of clear and particular identification of the polypeptide to which the claims are directed, the metes and bounds of the subject matter that Applicant regards as the invention are sufficiently delineated, so as to permit the skilled

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artisan to determine infringing and non-infringing subject matter and thereby satisfy the requirement set forth under 35 U.S.C. § 112, second paragraph.

This issue may be remedied by amending claim 1 to reference to the amino acid sequence of "migration stimulation factor" to which the claims are directed because the amino acid sequence of a polypeptide is a unique identifier that unambiguously defines a given polypeptide.

18. Claims 1, 4, 5, and 7 are rejected under 35 U.S.C. 112, first paragraph, because the specification, **while being enabling for making and using an *isolated*, recombinant nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, an *isolated*, recombinant nucleic acid molecule comprising the polynucleotide sequence of SEQ ID NO: 3, and an *isolated* replicable vector comprising the polynucleotide sequence of any of the aforementioned nucleic acid molecules, does not reasonably provide enablement for making and using any such *non-isolated* nucleic acid molecules or replicable vectors encompassed by the claims.** The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

As explained in the above rejection of claims 1, 4, 5, and 7 under 35 U.S.C. 101, the claims encompass the polynucleotides according to claim 1 or the replicable vectors (e.g., a recombinant retrovirus) according to claim 7, which have been introduced into cells comprised within an organism, including humans that are treated with such polynucleotides and replicable vectors. Again, support for this interpretation of the claims is found throughout the specification, as originally filed (e.g., page 12, line 23, through page 13, line 28; page 42, lines 6-8; and page 44, lines 10 and 11).

However, as explained in section 21 of the preceding Office action with regard to claim 8, the amount of guidance, direction, and exemplification set forth in the specification would not be sufficient to enable the skilled artisan to make and use the claimed invention without undue and/or unreasonable experimentation. This position was supported by the teachings of Houdebine (of record), Verma et al. (of record)

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Amalfitano et al. (of record), Pandha et al. (of record), and the memorandum dated January 14, 2003, by Dr. Patterson of the U.S. Department of Health and Human Services. This ground of rejection set forth in the preceding Office action is herein reiterated with respect to claims 1, 4, 5, and 7, as these claims are broadly but reasonably interpreted to encompass polynucleotides and replicable vectors comprising polynucleotide sequences encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, which have been introduced into cells of which animals, including humans are comprised.

Notably it would be remedial to amend claims 1, 4, 5, and 7 to recite the limitation "isolated" before "recombinant polynucleotide" or "replicable vector".

19. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

This is a "new matter" rejection.

Claim 1 recites, "wherein migration stimulation factor activity refers to ability to stimulate adult skin fibroblast migration into collagen gel".

At page 5 of the amendment filed November 11, 2005, Applicant has asserted that written support for the language of the claim 1 is found throughout the specification but, in particular, at page 9.

Although the specification, as originally filed, describes assessing the activity of members of a genus of "MSF polypeptides" in "bioassays based on its stimulation of adult skin fibroblast migration, for example, as in Picardo *et al* (1991) *The Lancet* 337, 130-133" (page 10, lines 1-6), this disclosure is insufficient to provide proper written support for defining the migration stimulation factor activity of the genus of polypeptides to which the claims are directed as "[the] ability to stimulate adult skin fibroblast migration **into collagen gel**" (emphasis added).

Furthermore, although the specification cites Picardo et al. as describing such a biosassay, MPEP § 608.01(p) does not provide for the incorporation by reference of essential material by reference to non-patent publications. "Essential material" is defined as "that which is necessary to (1) describe the claimed invention, (2) provide an enabling disclosure of the claimed invention, or (3) describe the best mode (35 U.S.C. 112)". The bioassay described by Picardo et al. is essential information because claim 1 presently recites, "wherein migration stimulation factor activity refers to ability to stimulate adult skin fibroblast migration into collagen gel", and thus the disclosure of Picardo et al. describing such a bioassay is necessary to describe, if not enable, the claimed invention.

It is suggested this issue may be remedied by incorporating relevant portions of the disclosure of Picardo et al. (of record), which provide sufficient written support for the present claim language. Applicant should do so by amending the specification to include this material incorporated by reference to Picardo et al., and the amendment must be accompanied by an affidavit or declaration executed by Applicant, or a practitioner representing Applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See *In re Hawkins*, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); *In re Hawkins*, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and *In re Hawkins*, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

### ***Claim Rejections - 35 USC § 102***

20. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.



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21. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,830,700 A, as evidenced by the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.mi" (i.e., Result 2), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Claim 1 is drawn to a recombinant polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, or alternatively to a polynucleotide having a sequence with at least 90% homology to a polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Claim 7 is drawn to a replicable vector comprising a recombinant polynucleotide according to claim 1. Claims 8 and 60 are drawn to an isolated host cell comprising a recombinant polynucleotide according to claim 1, or a replicable vector according to claim 7, respectively. Claims 9 and 61 are drawn to methods for making a polypeptide having at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2, said methods comprising culturing a host cell comprising a polynucleotide according to claim 1, or a host cell according to claim 60, respectively.

"Homology" is defined, for example, by Merriam-Webster Online Dictionary, which available on the Internet at <http://www.merriam-webster.com/>, as "similarity of nucleotide or amino-acid sequence in nucleic acids, peptides, or proteins" (copyright 2005 by Merriam-Webster, Incorporated). Homology or similarity of nucleic acid sequences may be evaluated by relatively subjective criterion, or it may be objectively measured using any of wide variety of differing criterion.

Accordingly, the claims are not limited to nucleic acid molecules comprising a polynucleotide sequence that is at least 90% identical to any particular polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2, such as the polynucleotide sequence of SEQ ID NO: 3. Rather the claims are directed to a genus of structurally varying nucleic acid molecules that are somehow determined to be 90%

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homologous (i.e., similar) to a polynucleotide sequence encoding the amino acid sequence of SEQ ID NO: 2

U.S. Patent No. 5,830,700 A (Irani) teaches an isolated, recombinant nucleic acid molecule comprising a polynucleotide that encodes a polypeptide that is 97.1% identical to amino acid sequence of SEQ ID NO: 2; see entire document (e.g., SEQ ID NO: 1). Irani teaches the polypeptide encoded by the disclosed nucleic acid molecule is produced by a process comprising culturing a host cell comprising a replicable vector comprising a polynucleotide sequence encoding the polypeptide and purifying the polypeptide; see, e.g., column 5, line 54, through column 8, line 44.

When compared to the polynucleotide sequence of SEQ ID NO: 3, which is the disclosed polynucleotide sequence encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, the polynucleotide sequence disclosed by the prior art has a "best local similarity" of 97.1%; see the attached copy of part of the U.S.P.T.O. search report "us-09-581-651d-3.rni" (Result 2), which was generated by searching the Office's "Issued Patents NA" database using SEQ ID NO: 3 as a query.

Although Irani et al. does not expressly teach the polypeptide encoded by the disclosed nucleic acid molecule has at least 30% of the "migration stimulation factor activity" of a polypeptide comprising SEQ ID NO: 2 and elicits antibodies that recognize "migration stimulation factor" but not fibronectin, the Office does not have the facilities for examining and comparing Applicant's product with the product of the prior art in order to establish that the product of the prior art does not possess the same material, structural, and functional characteristics as the claimed polynucleotide, replicable vector, and host cell, or for examining and comparing Applicant's process with process of the prior art to establish that the claimed method for making a polypeptide and the methods of the prior art produce distinguishable products.

Given the fact that the nucleic acid molecule disclosed by the prior art encodes a polypeptide having an amino acid sequence that is 94.8% identical to amino acid sequence of SEQ ID NO: 2, the claimed products and processes are deemed the same as those disclosed by the prior art, absent a showing of any difference.

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In the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

22. Claim 9 is rejected under 35 U.S.C. 102(b), as being anticipated by Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751.

Claim 9 is drawn to a method for making a polypeptide having at least 30% of the migration stimulation activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2, said method comprising culturing a host cell comprising a polynucleotide according to claim 1.

As explained in the below rejection of claim 1 under 35 U.S.C. § 101, claim 1 encompasses a naturally occurring nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the gene or messenger RNA (mRNA) transcribed from the gene encoding the polypeptide, which is expressed naturally in certain cells. As evidenced by Schor et al., GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, Grey et al. teaches culturing cells comprising such naturally occurring nucleic acid molecules encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2; see, e.g., page 2438, column 2, through page 2439, column 1. Grey et al. teaches isolating the polypeptide expressed by the cultured cells; see, e.g., page 2439, columns 1 and 2. Because the polypeptide comprises the amino acid sequence of SEQ ID NO: 2, it is expected to have at least 30% of the migration stimulation activity of the polypeptide having the amino acid sequence of SEQ ID NO: 2.

For further clarity, a polynucleotide according to claim 1 is not isolated, nor is it necessarily recombinant. Claim 1 is alternatively drawn a polynucleotide, albeit not necessarily recombinant, having a sequence with at least 90% homology to a

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polynucleotide encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2 and encoding a polypeptide that has at least 30% of the migration stimulation factor activity of a polypeptide comprising SEQ ID NO: 2 and which elicits antibodies that recognize "migration stimulation factor" but not fibronectin. Nevertheless, even if claim 1 is limited to a "recombinant" polynucleotide, as explained in greater depth and detail below in the rejection of claim 1 under 35 U.S.C. § 101, a "recombinant" polynucleotide cannot be distinguished from a naturally occurring nucleic acid molecule encoding a polypeptide comprising the amino acid sequence of SEQ ID NO: 2, such as the gene or mRNA transcribed from the gene encoding the polypeptide, which are found in the cells such as those disclosed by Grey et al.

In traversing the ground of rejection of claims under 35 U.S.C. § 102, as being anticipated by Grey et al., as evidenced by Schor et al. (*Cancer Res.* 2003 Dec; **63** (24): 8827-8836) (of record), which was set forth in the preceding Office action, Applicant argued that there is no evidence that Grey et al. necessarily discloses a protein having the amino acid sequence of SEQ ID NO: 2; see, e.g., page 13 of the amendment filed June 8, 2005. Moreover, Applicant contended the polypeptide disclosed by Grey et al. may not be the disclosed polypeptide having the amino acid sequence of SEQ ID NO: 2, since it could be another polypeptide, such as the polypeptide disclosed by database EMBL Accession No. AJ535086, which comprises 15 amino acids not present in the amino acid sequence of SEQ ID NO: 2, as depicted in Figure 2. Applicant stated the amino acid sequence encoded by the polynucleotide sequence of EMBL Accession No. AJ535086 is 657 amino acids in length, whereas the amino acid sequence depicted in Figure 2 (i.e., SEQ ID NO: 2) is only 642 amino acids.

Without acquiescing to Applicant's arguments, it is herein noted that Schor et al. (*Breast Cancer Res.* 2001; **3**: 373-379) teaches the polynucleotide sequence of a complementary DNA molecule encoding "MSF", the 70 kDa polypeptide first purified by Grey et al., was submitted to the database EMBL under the accession number AJ276395; see entire document (e.g., page 376, columns 1 and 2). According to EMBL/GenBank™ Accession No. AJ276395, the amino acid sequence that is encoded by the disclosed polynucleotide sequence is reported in database UniProtKB/Swiss-

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Prot™ under the accession number P02751. According to UniProtKB/Swiss-Prot™ Accession No. P02751, the amino acid sequence of the alternative splice form-2, designated "MSF FN-70" and described by Schor et al. (*Breast Cancer Res.* 2001; 3: 373-379)) is 642 amino acids.

The Examiner cannot account for the disparity between the amino acid sequence reported by Schor et al. as EMBL/GenBank™ Accession No. AJ276395 (i.e., the 642 amino acid sequence) and amino acid sequence, also reported by Schor et al., of EMBL Accession No. AJ535086 (i.e., the 657 amino acid sequence). Nevertheless, as evidenced by Schor et al. (*Breast Cancer Res.* 2001; 3: 373-379) and corresponding disclosures in the databases, it appears that the 70 kDa polypeptide produced by the fibroblasts cultured by Grey et al. is the polypeptide of SEQ ID NO: 2.

Again, in the absence of evidence to the contrary, the burden is upon the applicant to prove that the claimed products and processes are different than those taught by the prior art. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA, 1977) and *Ex parte Gray*, 10 USPQ2d 1922 1923 (PTO Board of Patent Appeals and Interferences, 1988 and 1989).

### ***Claim Rejections - 35 USC § 103***

23. Claims 1, 7-9, 60, and 61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Grey et al. (of record), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; 3: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, in view of Bendig (of record).

Grey et al. and Bendig teach that which is set forth in section 29 of the preceding Office action.

As explained in the above rejection of claim 9 under 35 U.S.C. 102(b), as evidenced by Schor et al. (*Breast Cancer Res.* 2001; 3: 373-379), GenBank™ Accession No. AJ276395, and UniProtKB/Swiss-Prot™ Accession No. P02751, the 70 kDa polypeptide designated "migration stimulation factor (MSF)", which was isolated from cultured fibroblasts by Grey et al., is the polypeptide of SEQ ID NO: 2.

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Grey et al. teaches, "[o]ur current efforts are directed toward cloning the gene for MSF and obtaining its complete sequence" (page 2441, column 1).

As explained in the preceding Office action, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time the invention was made to have cloned a nucleic acid molecule encoding the polypeptide disclosed by Grey et al. because Grey et al. teaches efforts are underway to do exactly that, and Bendig teaches the methodology necessary to do so was well within the skill of the artisan of ordinary skill at the time the invention was made. Accordingly, as also explained in the preceding Office action, it would have been *prima facie* obvious to one ordinarily skilled in the art at the time of the invention to produce a host cell comprising a vector comprising the cloned polynucleotide sequence encoding the polypeptide by recombinant DNA technology in accordance with the teachings reviewed by Bendig and then culture the host cells and isolate the polypeptide produced by the host cells in the culture. Therefore, among other reasons, one ordinarily skilled in the art at the time of the invention would have been motivated to do so to facilitate production of the polypeptide by recombinant means.

### ***Conclusion***


24. Claim 29 is allowed; no other claim is allowed.

25. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Larry Helms, Ph.D. can be reached on (571) 272-0832. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



Stephen L. Rawlings, Ph.D.  
Examiner  
Art Unit 1643

slr  
January 17, 2006

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## Alternative Splicing of entry: P02751

### Splice Isoform: 2

#### Isoform description

Name **2**

Synonyms **MSF-FN70, Migration stimulation factor FN70**

Isoform ID **P02751-2**

Features which should be applied to build the isoform sequence: **VSP\_003255, VSP\_003256, VSP\_003257**

#### Sequence information

Length: **642 AA**

10	20	30	40	50	60
MLRGPGPGLL	LLAVQCLGTA	VPSTGASKSK	RQAQQMVPQ	SPVAVSQSKP	GCYDNGKHYQ
70	80	90	100	110	120
INQQWERTYL	GNALVCTCYG	GSRGFNCESK	PEAEETCFDK	YTGNTYRVGD	TYERPKDSMI
130	140	150	160	170	180
WDCTCIGAGR	GRISCTIANR	CHEGGQSYKI	GDTWRRPHET	GGYMLECVCL	GNGKGEWTCK
190	200	210	220	230	240
PIAEKCFDHA	AGTSYVVGET	WEKPYQGMM	VDCTCLGEGS	GRITCTSRNR	CNDQDTRTSY
250	260	270	280	290	300
RIGDTWSKKD	NRGNLLQCIC	TGNRGGEWKC	ERHTSVQTTS	SGSGPFTDVR	AAVYQPQPHP
310	320	330	340	350	360
QPPPYGHCVT	DSGVVYSVGM	QWLKTQGNKQ	MLCTCLGNGV	SCQETAVTQT	YGGNSNGEPC



370	380	390	400	410	420
VLPFTYNDRT	DSTTSNYEQD	QKYSFCTDHT	VLVQTQGGNS	NGALCHFPFL	YNNHNYTDCT
430	440	450	460	470	480
SEGRRDNMKW	CGTTQNYDAD	QKFGFCPMAA	HEEICTTNEG	VMYRIGDQWD	KQHDMGHMMR
490	500	510	520	530	540
CTCVGNRGE	WTCIAYSQLR	DQCIVDDITY	NVNDTFHKRH	EEGHMLNCTC	FGQGRGRWKC
550	560	570	580	590	600
DPVDQCQDSE	TGTFYQIGDS	WEKYVHGVRY	QCYCYGRGIG	EWHCQPLQTY	PSSSGPVEVF
610	620	630	640		
ITETPSQPNS	HPIQWNAPQP	SHISKYILRW	RPVSIPPRNL	GY	

**BLAST**

BLAST submission on  
ExPASy/SIB  
or at NCBI (USA)



Sequence analysis tools: ProtParam,  
ProtScale, Compute pI/Mw, PeptideMass,  
PeptideCutter, Dotlet (Java)



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OM nucleic - nucleic search, using sw model

Run on: November 10, 2005, 22:35:24 ; Search time 367 Seconds

(without alignments)  
9572.442 Million cell updates/sec

Title: US-09-581-651D-3

Perfect score: 2147

Sequence: 1 caaacttggtggaacttgc.....aaaaaaaaaaaaaaaaaaaaa 2147

Scoring table: IDENTITY\_NUC

Gapop 10.0 , Gapext 1.0

Searched: 1202784 seqs, 818138359 residues

Total number of hits satisfying chosen parameters: 2405568

Minimum DB seq length: 0

Maximum DB seq length: 2000000000

Post-processing: Minimum Match 0%

Listing first 45 summaries

Database :

Issued Patents NA: \*  
1: /cgn2\_6/prodata/1/ina/5A\_COMB.seq: \*  
2: /cgn2\_6/prodata/1/ina/5B\_COMB.seq: \*  
3: /cgn2\_6/prodata/1/ina/6A\_COMB.seq: \*  
4: /cgn2\_6/prodata/1/ina/6B\_COMB.seq: \*  
5: /cgn2\_6/prodata/1/ina/6C\_COMB.seq: \*  
6: /cgn2\_6/prodata/1/ina/backfiles1.seq: \*

Pred. No. is the number of results predicted by chance to have a score greater than or equal to the score of the result being printed, and is derived by analysis of the total score distribution.

# SUMMARIES

Result No.	Score	Query Match	Length	DB ID	Description
1	1887.4	87.9	8044	4	US-09-566-921-135
2	1826.8	85.1	7803	2	US-08-551-356-1
3	1826.8	85.1	7803	5	PCT-US93-12687-1
4	1743.4	81.2	7679	4	US-09-220-132-38
5	1743.4	81.2	7680	4	US-09-023-655-1289
6	1743.4	81.2	7680	5	PCT-US95-09819-6
7	1740.2	81.1	7705	1	US-08-259-569-16
8	1740.2	81.1	7705	2	US-08-826-885-16
9	1738.6	81.0	7705	6	5455158-2
10	1738.6	81.0	7705	6	5455158-2
11	671.2	31.3	596	1	US-07-637-250A-8
12	671.2	31.3	596	1	US-08-145-061-8
13	97.4	4.5	186	1	US-08-153-799-5
14	73.8	3.4	2109	4	US-09-799-451-345
15	73.8	3.4	2334	4	US-09-023-655-996
16	73.8	3.4	2334	4	US-09-949-016-704
17	73.8	3.4	2335	4	US-09-799-451-346
18	73.8	3.4	2335	4	US-09-949-016-4758
19	73.2	3.4	11665	4	US-09-949-016-12446
20	73.2	3.4	11665	4	US-09-949-016-16500
21	72.4	3.4	85	1	US-08-259-569-28
22	72.4	3.4	85	2	US-08-826-885-28
23	72.2	3.4	2334	1	US-08-457-304A-33
24	72.2	3.4	2334	1	US-08-456-701A-33
25	72.2	3.4	2334	3	US-08-684-932A-33
26	72	3.4	72	1	US-08-259-569-29
27	72	3.4	72	2	US-08-826-885-29

28	72	3.4	72	6	5455158-9	Patent No. 5455158
29	72	3.4	72	6	5455158-9	Patent No. 5455158
30	71.8	3.3	1983	4	US-09-949-016-2066	Sequence 2066, Ap
31	71.8	3.3	3069	4	US-09-949-016-641	Sequence 641, App
32	69	3.2	69	1	US-08-259-569-23	Sequence 23, Appl
33	69	3.2	69	2	US-08-826-885-23	Sequence 23, Appl
34	65.8	3.1	69	6	5455158-6	Patent No. 5455158
35	65.8	3.1	69	6	5455158-6	Patent No. 5455158
36	65.4	3.0	69	1	US-08-259-569-30	Sequence 30, Appl
37	65.4	3.0	69	2	US-08-826-885-30	Sequence 30, Appl
38	65.2	3.0	601	4	US-09-949-016-30391	Sequence 30391, A
39	65.2	3.0	601	4	US-09-949-016-70165	Sequence 70165, A
40	65.2	3.0	29954	4	US-09-949-016-13808	Sequence 13808, A
41	65.2	3.0	31040	4	US-09-949-016-12383	Sequence 12383, A
42	65	3.0	75	1	US-08-259-569-18	Sequence 18, Appl
43	65	3.0	75	2	US-08-826-885-18	Sequence 18, Appl
44	64.8	3.0	68	6	5455158-4	Patent No. 5455158
45	64.8	3.0	68	6	5455158-4	Patent No. 5455158

## ALIGNMENTS

### RESULT 1

US-09-566-921-135  
; Sequence 135, Application US/09566921  
; Patent No. 6682888  
; GENERAL INFORMATION:  
; APPLICANT: Loring, Jeanne F.  
; APPLICANT: Tingley, Debora W.  
; APPLICANT: Edwards, Carla M.  
; TITLE OF INVENTION: GENES EXPRESSED IN ALZHEIMER'S DISEASE  
; FILE REFERENCE: PA-0024 US  
; CURRENT APPLICATION NUMBER: US/09/566,921  
; CURRENT FILING DATE: 2000-05-05  
; NUMBER OF SEQ ID NOS: 138  
; SOFTWARE: PERL Program  
; SEQ ID NO 135  
; LENGTH: 8044  
; TYPE: DNA  
; ORGANISM: Homo sapiens  
; FEATURE:  
; NAME/KEY: misc feature  
; OTHER INFORMATION: Incyte ID No. 6682888 427813.14  
US-09-566-921-135

Query Match	87.9%	Score	1887.4	DB	4	Length	8044
Best Local Similarity	97.4%	Pred. No.	0				
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QY	1	CAAACCTTGTCGCAACTTGCCTCCCGGTCGGGGCGTCTCTCCCGCACCGTCTCAACATGC	60				
DB	213	CAAACCTTGTCGCAACTTGCCTCCCGGTCGGGGCGTCTCTCCCGCACCGTCTCAACATGC	272				
QY	61	TTAGGGGTCGGGGCGGCGGTCGTCGTCGCGCGTCCAGTCCGTCGGGACAGCGGTGC	120				
DB	273	TTAGGGGTCGGGGCGGCGGTCGTCGTCGCGCGTCCAGTCCGTCGGGACAGCGGTGC	332				
QY	121	CCTCCACGGGAGCCTCGAAGAGCAAGAGCAGGCTCAGCAATGGTTTCAGCCCCAGTCCC	180				
DB	333	CCTCCACGGGAGCCTCGAAGAGCAAGAGCAGGCTCAGCAATGGTTTCAGCCCCAGTCCC	392				
QY	181	CGGTGGCTGTCAGTCAAGCAAGCCCGGTTGTTATGCAATGGAAGAACTATCAGATAA	240				
DB	393	CGGTGGCTGTCAGTCAAGCAAGCCCGGTTGTTATGCAATGGAAGAACTATCAGATAA	452				
QY	241	ATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGTTGTTACTTCTTATGGAGAA	300				
DB	453	ATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTTGTTGTTACTTCTTATGGAGAA	512				
QY	301	GCCGAGGTTTTAACTGCGAGAGATAAACCTGGAAGACTTGTCTTGAACAAGTACA	360				
DB	513	GCCGAGGTTTTAACTGCGAGAGATAAACCTGGAAGACTTGTCTTGAACAAGTACA	572				

QY	361	CTGGGAAACCTTACCGAGTGGGTGACCTTATGAGCGTCTTAAAGACTCCATGATCTGGG	420
DB	573	CTGGGAAACCTTACCGAGTGGGTGACCTTATGAGCGTCTTAAAGACTCCATGATCTGGG	632
QY	421	ACTGTACCTTGCATCGGGGCTTGGCGAGGGAGATAAGCTGTATCCATCGCAAAACCGCTGCC	480
DB	633	ACTGTACCTTGCATTTGGGGCTTGGCGAGGGAGATAAGCTGTATCCATCGCAAAACCGCTGCC	692
QY	481	ATGAAGGGGGTCAGTCTCTCAAGATTGGTGACACCTTGGAGGAGACCACTATGAGACTGGTG	540
DB	693	ATGAAGGGGGTCAGTCTCTCAAGATTGGTGACACCTTGGAGGAGACCACTATGAGACTGGTG	752
QY	541	GTTACATGTTAGAGTGTGTGTCTTGGTAAATGCAAAAAGAGAAATGGAATCTGCAAGCCCA	600
DB	753	GTTACATGTTAGAGTGTGTGTCTTGGTAAATGCAAAAAGAGAAATGGAATCTGCAAGCCCA	812
QY	601	TAGCTGGAAGTGTGTTTTGATCATGCTGCTGGGACTTCTTATGTGGTGGAGAAAACGTGGG	660
DB	813	TAGCTGGAAGTGTGTTTTGATCATGCTGCTGGGACTTCTTATGTGGTGGAGAAAACGTGGG	872
QY	661	AGAAGCCCTACCAAGGCTGGATGATGTATGTACTTTGCCCTGGGAGAGGAGCGGAC	720
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QY	721	GCATCATTTGCACTTTAGAAAATAGATGCAACGATCAGGACACAAGGACATCTCTATAGAA	780
DB	933	GCATCATTTGCACTTTAGAAAATAGATGCAACGATCAGGACACAAGGACATCTCTATAGAA	992
QY	781	TTGGAGACACTTGGAGCAGAAGGATTAATCGAGGAAACCTGCTCAGTGCATCTGCACACAG	840
DB	993	TTGGAGACACTTGGAGCAGAAGGATTAATCGAGGAAACCTGCTCAGTGCATCTGCACACAG	1052
QY	841	GCAACGGCCGAGGAGTGGAAAGTGTGAGAGGCACACCTCTGTGCAGACACCATCGAGCG	900
DB	1053	GCAACGGCCGAGGAGTGGAAAGTGTGAGAGGCACACCTCTGTGCAGACACCATCGAGCG	1112
QY	901	GATCTGGCCCTTACCCGATGTTCTGCAGCTGTTTACGAAACCGCAGCCTCACCCCCAGC	960
DB	1113	GATCTGGCCCTTACCCGATGTTCTGCAGCTGTTTACGAAACCGCAGCCTCACCCCCAGC	1172
QY	961	CTCTCTCCCTATGGCCACTGTGTACAGACAGTGGTGGTGTCTACTCTGTGGGAGATGCAGT	1020
DB	1173	CTCTCTCCCTATGGCCACTGTGTACAGACAGTGGTGGTGTCTACTCTGTGGGAGATGCAGT	1232
QY	1021	GGCTGAAGACACAAGGAAATAAGCAAAATGCTTTTGACGTGCTGGGCAACGGAGTCAGCT	1080
DB	1233	GGCTGAAGACACAAGGAAATAAGCAAAATGCTTTTGACGTGCTGGGCAACGGAGTCAGCT	1292
QY	1081	GCCAAAGACAGCTGTAAACCCAGACTTACCGTGGCAACTCAATATGAGAGCCATGTGTCT	1140
DB	1293	GCCAAAGACAGCTGTAAACCCAGACTTACCGTGGCAACTCAATATGAGAGCCATGTGTCT	1352
QY	1141	TACCATTTCCTTACAACGACGAGGAC-----	1165
DB	1353	TACCAATTCACTCAATATGGCAGGAGCTTCTACTCTGCAACCAAGAGGGGACAGGACG	1412
QY	1166	-----GGACAGCACAACTTCGAATTATGAGCAGGACCAAGAAATACTCTTTCTGCA	1215
DB	1413	GACATCTTTGGTGAGCACAACTTCGAATTATGAGCAGGACCAAGAAATACTCTTTCTGCA	1472
QY	1216	CAGACCAACATGTTTTGGTTCAGACTCGAGGAGGAATTCCAATGGTGCCCTTGGCCACT	1275
DB	1473	CAGACCAACATGTTTTGGTTCAGACTCGAGGAGGAATTCCAATGGTGCCCTTGGCCACT	1532
QY	1276	TCCCTCTCTTACAAACCAAAATTAACACTGATTCGACTTCTGAGGGCAGAGAGACA	1335
DB	1533	TCCCTCTCTTACAAACCAAAATTAACACTGATTCGACTTCTGAGGGCAGAGAGACA	1592
QY	1336	ACATGAAGTGTGGGACCAACAGAACTATATGATCCGACCAAGAGTTTGGGTTCTGCC	1395
DB	1593	ACATGAAGTGTGGGACCAACAGAACTATATGATCCGACCAAGAGTTTGGGTTCTGCC	1652

BRSH.T 2

RESÚLTADO 2  
IIS-08-551-356-1US-08-551-356-1  
: Sequence 1 Application US/08551356

; Sequence 1, Application No. 5830700

Patent No. 5830700  
GENERAL INFORMATION:

GENERAL INFORMATION:

APPLICANT: Irani, Meher

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; NUMBER OF SEQUENCES: 14  
CORRELATION COEFFICIENT: .986000

CORRESPONDENCE ADDRESS:

ADDRESS: ZymoGenetics, Inc.

STREET: 4225

; CITY: Seat ...

STATB: WA

COUNTRY: U.S.

ZIP: 98105

; COMPUTER READABLE FORM:

MEDIUM TYPE: Floppy disk

COMPUTER: IBM PC compatible

**OPERATING SYSTEM:** PC-DOS/MS-DOS

SOFTWARE: PatentIn Rel

; SOFTWARE. TECHNICAL RECORDS #12167  
; CURRENT APPLICATION DATA:

APPROPRIATE AGENCY

; AFFIDAVIT NUMBER:  
 ; FILING DATE:

FILED DATE: 435  
CLASSIFICATION: 435

CLASSIFICATION: 433  
PRIOR APPLICATION DATA:

;  
;  
;  
;

;  
 ; APPLICATION NUMBER: US/08/343,762  
 ; FILING DATE:

FILING DATE: 11/11/2011  
APPLICATION: 11/11/2011

APPLICANT NUMBER: 05/0

;  
FILING DATE:  
ATTORNEY / AGENT

ATTORNEY/AGENT INFORMATION:  
NAME: HOLLY JULIE A



	Qy	1927	CCAGTACATTTCTCAGGTGGAGACT	1952
	Dβ	1921	CCAGTACATTTCTCAGGTGGAGACT	1946

### RESULT 3

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PCT-US93-12687-1
; Sequence 1, Application PC/TUS9312687
; GENERAL INFORMATION:
; APPLICANT: Iran1, Meher H.
; TITLE OF INVENTION: HYBRID CROSS-LINKING PROTEINS
; NUMBER OF SEQUENCES: 14
; CORRESPONDENCE ADDRESS:
; ADDRESSEE: ZymGenetics, Inc.
; STREET: 4225 Roosevelt Way, N.E.
; CITY: Seattle
; STATE: WA
; COUNTRY: USA
; ZIP: 98105
; COMPUTER READABLE FORM:
; MEDIUM TYPE: Floppy disk
; COMPUTER: IBM PC compatible
; OPERATING SYSTEM: PC-DOS/MS-DOS
; SOFTWARE: PatentIn Release #1.0, Version #1.25
; CURRENT APPLICATION DATA:
; APPLICATION NUMBER: PCT/US93/12687
; FILING DATE:
; CLASSIFICATION:
; PRIOR APPLICATION DATA:
; APPLICATION NUMBER: US 07/998, 271
; FILING DATE: 31-DEC-1992
; ATTORNEY/AGENT INFORMATION:
; NAME: Parker, Gary E
; REGISTRATION NUMBER: 31-648
; REFERENCE/DOCKET NUMBER: 92-26PC
; TELECOMMUNICATION INFORMATION:
; TELEPHONE: 206-547-8080 ext 322
; TELEFAX: 206-548-2329
; INFORMATION FOR SEQ ID NO: 1:
; SEQUENCE CHARACTERISTICS:
; LENGTH: 7803 base pairs
; TYPE: nucleic acid
; STRANDEDNESS: single
; TOPOLOGY: linear
; FEATURE:
; NAME/KEY: CDS
; LOCATION: 6..7346
; PCT-US93-12687-1

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Query Match	85.1%	Score 1826.8	DB 5	Length 7803	
Best Local Similarity	97.1%	Prod. No. 0			
Matches 1889	Conservative	0	Mismatches 12	Indels 45	Gaps 1
Qy	52	TCAACATGCTTTAGGGGTCCGGGGCCCGGGCTGTGCTGTCTGGCCGTCCAGTGCCTGGGGA	111		
Db	1	TCAACATGCTTTAGGGGTCCGGGGCCCGGGCTGTGCTGTCTGGCCGTCTGTGCTGGGGA	60		
Qy	112	CAGCGGTGCTCTCCACGGGAGCCTCGAAGACGACGAGCAGCGCTCAGCAATGCTTCAGC	171		
Db	61	CAGCGGTGCTCTCCACGGGAGCCTCGAAGACGACGAGCAGCGCTCAGCAATGCTTCAGC	120		
Qy	172	CCCAGTCCCGGTGGCTGTCAAGTCAAGCAGCCCGTGTGTTATGACAAATGGAACAACCT	231		
Db	121	CCCAGTCCCGGTGGCTGTCAAGTCAAGCAGCCCGTGTGTTATGACAAATGGAACAACCT	180		
Qy	232	ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGCAATGCGTGGTGTGTACTTGTT	291		
Db	181	ATCAGATAAATCAACAGTGGGAGCGGACCTACCTAGGTAATGTGTGTGTTGTACTTGTT	240		
Qy	292	ATGAGGGAAGCCGAGGTTTTAACTCGAGAGTAAACCTGGAAGCTGAAGAGACTTGCTTTG	351		
Db	241	ATGAGGGAAGCCGAGGTTTTAACTCGAAGTAAACCTGGAAGCTGAAGAGACTTGCTTTG	300		

QY	352	ACAAGTACATCGGGAACA	CTTACCGAGTGGGTGAC	CACTTATGAGCGTCTTAAAGACTCCA	411
DB	301	ACAAGTACATCGGGAACA	CTTACCGAGTGGGTGAC	CACTTATGAGCGTCTTAAAGACTCCA	360
QY	412	TGATCTGGGACTGTACCT	TCGCAATCGGGGCTGGCGAGGAGAA	TAAAGCTGTACCATCGCAA	471
DB	361	TGATCTGGGACTGTACCT	TCGCAATCGGGGCTGGCGAGGAGAA	TAAAGCTGTACCATCGCAA	420
QY	472	ACCGTGCATGAAGGGGGT	CAGTCC	TACAGATTGGTGACACCTCGGAGGAGACCACATG	531
DB	421	ACCGTGCATGAAGGGGGT	CAGTCC	TACAGATTGGTGACACCTCGGAGGAGACCACATG	480
QY	532	AGACTGGTGGTTACATG	TTTAGAGTGTGTGCTTGTG	TAAATGGAAGGAGAAATGGACCT	591
DB	481	AGACTGGTGGTTACATG	TTTAGAGTGTGTGCTTGTG	TAAATGGAAGGAGAAATGGACCT	540
QY	592	GCAAGCCCATAGCTGAGA	AGTGT	TTTGATCATGCTGCTGGGACTTCTTATGTGGTCGGAG	651
DB	541	GCAAGCCCATAGCTGAGA	AGTGT	TTTGATCATGCTGCTGGGACTTCTTATGTGGTCGGAG	600
QY	652	AAACGTGGGAGAGCCCT	TACCAAGGCTCGATGATGTAG	TGTACTTGGCCCTGGGAGAAG	711
DB	601	AAACGTGGGAGAGCCCT	TACCAAGGCTCGATGATGTAG	TGTACTTGGCCCTGGGAGAAG	660
QY	712	GCAGCGGACGCATCACT	TGSCACTTCTAGAAATAGAT	TGCACGATCAGGACACAAGGACAT	771
DB	661	GCAGCGGACGCATCACT	TGSCACTTCTAGAAATAGAT	TGCACGATCAGGACACAAGGACAT	720
QY	772	CCATATGAATTTGAGACA	CACTCGGAGCAGAGAGGAT	TAAATCGAGGAAACCTGCTCCAGTGCA	831
DB	721	CCATATGAATTTGAGACA	CACTCGGAGCAGAGAGGAT	TAAATCGAGGAAACCTGCTCCAGTGCA	780
QY	832	TCGTCACAGCAACGGC	CGAGGAGAGTGGAA	GTGTGAGAGGCACACCTCTGTGCGAGACCA	891
DB	781	TCGTCACAGCAACGGC	CGAGGAGAGTGGAA	GTGTGAGAGGCACACCTCTGTGCGAGACCA	840
QY	892	CATCGAGCGGATCTG	CGCCCTTCA	CGGATGTGTGTCAGCTGTTTACCAACCGCAGCCCTC	951
DB	841	CATCGAGCGGATCTG	CGCCCTTCA	CGGATGTGTGTCAGCTGTTTACCAACCGCAGCCCTC	900
QY	952	ACCCCGAGCTCTCC	TATGCCACATG	TGTCACAGACAGTGTGTGTGCTTACTCTGTGG	1011
DB	901	ACCCCGAGCTCTCC	TATGCCACATG	TGTCACAGACAGTGTGTGTGCTTACTCTGTGG	960
QY	1012	GGATGCAGTGGCTG	GAAGACACAAGG	AAATGAACAAATGCTTTTGACGTGCTGGGCAACG	1071
DB	961	GGATGCAGTGGCTG	GAAGACACAAGG	AAATGAACAAATGCTTTTGACGTGCTGGGCAACG	1020
QY	1072	GAGTCAAGTCCCAAG	AGACAGCTGTAA	CCGAGCTTACCGTGGCAACTCAATGGGAGGC	1131
DB	1021	GAGTCAAGTCCCAAG	AGACAGCTGTAA	CCGAGCTTACCGTGGCAACTCAATGGGAGGC	1080
QY	1132	CATGTGTCTTACCAT	TTCACTCA	CAAGCAGGAGC-----	1165
DB	1081	CATGTGTCTTACCAT	TTCACTCA	CAAGCAGGAGC-----	1140
QY	1166	-----	GGACAGACAACT	TTGAAATATGAGCAGGACCAAGAAATACT	1206
DB	1141	GACAGGACGGACAT	CTTTGGTGCAGCACA	CAACTTGAATATGAGCAGGACCAAGAAATACT	1200
QY	1207	CTTTCTGCA	CAGACCA	CACTGTTTGGTTCAGACTCGAGGAGGAAATCCAAATGGTGCCT	1266
DB	1201	CTTTCTGCA	CAGACCA	CACTGTTTGGTTCAGACTCAAGGAGGAAATCCAAATGGTGCCT	1260
QY	1267	TGTGCCACTTCCCT	CTTATACAA	CAACCAATTAACATGTCACCTTCTGAGGGCA	1326
DB	1261	TGTGCCACTTCCCT	CTTATACAA	CAACCAATTAACATGTCACCTTCTGAGGGCA	1320
QY	1327	GAAGAGACA	ATGAAGTGTGTGG	ACCAACAAGATATGATGCGGACCAAGATTTTG	1386
DB	1321	GAAGAGACA	ATGAAGTGTGTGG	ACCAACAAGATATGATGCGGACCAAGATTTTG	1380

1387 GGTCTCTGCCCATGGCTGCCACAGAGAAATCTGCACAAACCAATGAAGGGTCATGTACC 1446  
Db |||||  
1381 GGTCTCTGCCCATGGCTGCCACAGAGAAATCTGCACAAACCAATGAAGGGTCATGTACC 1440  
Db |||||  
1447 GCATTGGAGATCAGTGGGTAAGACGACATGACATGGGTCAATGATGAGGTGCAGTGTG 1506  
Qy |||||  
1441 GCATTGGAGATCAGTGGGTAAGACGACATGACATGGGTCAATGATGAGGTGCAGTGTG 1500  
Db |||||  
1507 TTGGGAATGGTGGTGGGTAAGACGACATGATGGCTTACCTGACGATTCGAGATCAGTGCA 1566  
Qy |||||  
1501 TTGGGAATGGTGGTGGGTAAGACGACATGATGGCTTACCTGACGATTCGAGATCAGTGCA 1560  
Db |||||  
1567 TTGTTGATGACATCACTTACATGTGAACGACACATTCACAAAGGCTCATGAAGAGGGGC 1626  
Qy |||||  
1561 TTGTTGATGACATCACTTACATGTGAACGACACATTCACAAAGGCTCATGAAGAGGGGC 1620  
Db |||||  
1627 ACATGCTGAATGATACATGCTTGGTCAAGGTGCGGGCAGGTGGAAGTGTGATCCCGTGG 1686  
Qy |||||  
1621 ACATGCTGAATGATACATGCTTGGTCAAGGTGCGGGCAGGTGGAAGTGTGATCCCGTGG 1680  
Db |||||  
1687 ACCAATGCCAGATTCAGAGCTGGGAGCTTTTATCAAAATGGAGATTCATGGGAGAAAT 1746  
Qy |||||  
1681 ACCAATGCCAGATTCAGAGCTGGGAGCTTTTATCAAAATGGAGATTCATGGGAGAAAT 1740  
Db |||||  
1747 ATGTGATGCTGTCAGATACCAATGCTACTGCTATGGCCGCTGGCATTTGGGGAGTGGCAT 1806  
Qy |||||  
1741 ATGTGATGCTGTCAGATACCAATGCTACTGCTATGGCCGCTGGCATTTGGGGAGTGGCAT 1800  
Db |||||  
1807 GCCAACTTTACAGACCTTCAAGCTCAAGTGGTCTGTCGAAGTATTTATCACTGAGA 1866  
Qy |||||  
1801 GCCAACTTTACAGACCTTCAAGCTCAAGTGGTCTGTCGAAGTATTTATCACTGAGA 1860  
Db |||||  
1867 CTCGAGTCAGCCCACTCCACCCATCCAGTGGATGGAATGACACAGCCATTCATTT 1926  
Qy |||||  
1861 CTCGAGTCAGCCCACTCCACCCATCCAGTGGATGGAATGACACAGCCATTCATTT 1920  
Db |||||  
1927 CCAAGTACATTCCTCAGTGGAGACCT 1952  
Qy |||||  
1921 CCAAGTACATTCCTCAGTGGAGACCT 1946  
Db |||||

## RESULT 4

US-09-220-132-38  
; Sequence 38, Application US/09220132  
; Patent No. 6506607  
; GENERAL INFORMATION:  
; APPLICANT: Shyjan, Andrew W.  
; TITLE OF INVENTION: METHODS AND COMPOSITIONS FOR THE IDENTIFICATION AND ASSESSMENT  
; OF PROSTATE CANCER THERAPIES AND THE DIAGNOSIS OF PROSTATE CANCER  
; FILE REFERENCE: 07334-074001  
; CURRENT APPLICATION NUMBER: US/09/220,132  
; CURRENT FILING DATE: 1998-12-23  
; PRIOR APPLICATION NUMBER: US 60/079,303  
; PRIOR FILING DATE: 1998-03-25  
; PRIOR APPLICATION NUMBER: US 60/068,821  
; PRIOR FILING DATE: 1997-12-24  
; NUMBER OF SEQ ID NOS: 191  
; SOFTWARE: FastSeq for Windows Version 4.0  
; SEQ ID NO 38  
; LENGTH: 7679  
; TYPE: DNA  
; ORGANISM: Homo sapiens  
US-09-220-132-38

Query Match 81.2%; Score 1743.4; DB 4; Length 7679;  
Best Local Similarity 97.0%; Pred. No. 0;  
Matches 1805; Conservative 0; Mismatches 11; Indels 45; Gaps 1;  
Qy 137 GAAGAGCAAGAGCGGCTCAGCAATGTTGAGCCCGGTCAGTGTGCTGTCAGTCA 196  
Db 1 GAAGAGCAAGAGCGGCTCAGCAATGTTGAGCCCGGTCAGTGTGCTGTCAGTCA 60  
Qy 197 AAGCAAGCCCGTGTGATGACATCGAAGAAACACTATCATAGATAAATCAACAGTGGGAGCG 256

61 AAGCAAGCCCGTGTGATGACATCGAAGAAACACTATCATAGATAAATCAACAGTGGAGCG 120  
Qy |||||  
257 GACCTACCTAGGCAATCGTTGGTTGTACTTGTATGAGAGAACCGAGGTTTTAACTG 316  
Db |||||  
121 GACCTACCTAGGCAATCGTTGGTTGTACTTGTATGAGAGAACCGAGGTTTTAACTG 180  
Qy |||||  
317 CGAGAGTAAACCTGAGCTGAGAGACTTGTGTTGACAAAGTACACTGGGAACACTTACCG 376  
Db |||||  
181 CGAAGTAAACCTGAGCTGAGAGACTTGTGTTGACAAAGTACACTGGGAACACTTACCG 240  
Qy |||||  
377 AGTGGGTGACACTTATGAGCGTCTTAAAGACTTCCATGATCTGGGACTGTACCTGATCGG 436  
Db |||||  
241 AGTGGGTGACACTTATGAGCGTCTTAAAGACTTCCATGATCTGGGACTGTACCTGATCGG 300  
Qy |||||  
437 GGTGGGCGAGGGAATAAGCTGTATCCATCGCAAAACCGCTGCCATGAAGGGGTGAGTC 496  
Db |||||  
301 GGTGGGCGAGGGAATAAGCTGTATCCATCGCAAAACCGCTGCCATGAAGGGGTGAGTC 360  
Qy |||||  
497 CTACAAGATTGGTGAACACTCTGGAGGAGACCATGAGACTGGTGTACATGTTAGAGTG 556  
Db |||||  
361 CTACAAGATTGGTGAACACTCTGGAGGAGACCATGAGACTGGTGTACATGTTAGAGTG 420  
Qy |||||  
557 TGTGTCTCTGTAATGGAAGGAGATGACCTGCAAGCCCATAGCTGAGAACTGTTT 616  
Db |||||  
421 TGTGTCTCTGTAATGGAAGGAGATGACCTGCAAGCCCATAGCTGAGAACTGTTT 480  
Qy |||||  
617 TGATCATGCTCTGGGACTTCTATGTTGGTGGGAGAAACGTGGGAGAACCTTACCAAGG 676  
Db |||||  
481 TGATCATGCTCTGGGACTTCTATGTTGGTGGGAGAAACGTGGGAGAACCTTACCAAGG 540  
Qy |||||  
677 CTGATGATGTTAGATTGTACTTGGCTGGGAGAGGCGGACGCATCATTGACATTC 736  
Db |||||  
541 CTGATGATGTTAGATTGTACTTGGCTGGGAGAGGCGGACGCATCATTGACATTC 600  
Qy |||||  
737 TAGAAATAGATCAACCATCAGGACACAAAGGACATCTTATAGAAATTTGGAGACACCTGGAG 796  
Db |||||  
601 TAGAAATAGATCAACCATCAGGACACAAAGGACATCTTATAGAAATTTGGAGACACCTGGAG 660  
Qy |||||  
797 CAAGAAGATTAATCGAGAAACCTGCTCAGTGCATCTGCAAGGCAACCGGCGGAGGAGA 856  
Db |||||  
661 CAAGAAGATTAATCGAGAAACCTGCTCAGTGCATCTGCAAGGCAACCGGCGGAGGAGA 720  
Qy |||||  
857 GTGGAAGTGTGAGAGGACACCTCTGTGACACCAATCGAGCGGATCTGGCCCTTAC 916  
Db |||||  
721 GTGGAAGTGTGAGAGGACACCTCTGTGACACCAATCGAGCGGATCTGGCCCTTAC 780  
Qy |||||  
917 CGATGTTCTGTCAGCTGTTTACCAACCGCAGCTCACCCCGAGCCCTCTCCCTATGGCCA 976  
Db |||||  
781 CGATGTTCTGTCAGCTGTTTACCAACCGCAGCTCACCCCGAGCCCTCTCCCTATGGCCA 840  
Qy |||||  
977 CTGTGTCAACAGATGTTGTTCTACTCTGTGGGATGAGTGGCTGGAAGACACAAGG 1036  
Db |||||  
841 CTGTGTCAACAGATGTTGTTCTACTCTGTGGGATGAGTGGCTGGAAGACACAAGG 900  
Qy |||||  
1037 AAATAGCAAAATGCTTGTGACGCTGGGCAACCGAGTCACTGCCAAGACAGCTGT 1096  
Db |||||  
901 AAATAGCAAAATGCTTGTGACGCTGGGCAACCGAGTCACTGCCAAGACAGCTGT 960  
Qy |||||  
1097 AACCCAGACTTACGTTGGCAACTCAATGGAAGAGCCATGTGTCTTACATTCACCTACAA 1156  
Db |||||  
961 AACCCAGACTTACGTTGGCAACTCAATGGAAGAGCCATGTGTCTTACATTCACCTACAA 1020  
Qy |||||  
1157 CGACAGGAC-----GGACAG 1171  
Db |||||  
1021 TGGCAGGAGCTTCTACTCTGCAACCGAAGGGGCGACAGGAGCATCTTTGGTGCAG 1080  
Qy |||||  
1172 CACAACCTTGAATTTATGAGCAGGACCAATATCTTTCTGCAAGACCACTGTTT 1231  
Db |||||  
1081 CACAACCTTGAATTTATGAGCAGGACCAATATCTTTCTGCAAGACCACTGTTT 1140  
Qy |||||  
1232 GGTTCAGACTCGAGGAGAAATTCATGTTGGCTTGTGCGCACTTCCCTCTTCTATACAA 1291  
Db |||||

Db 1141 GGTTCAGACTCAAGGAGAAATTCAAATGGTGCCTTGTGCGCACTTCCCTTCTCTATACAA 1200  
QY 1292 CAACACATTTACATGATGCTCTCTGAGGCGAGAGAGACACATGAACTGTGTGG 1351  
Db 1201 CAACACATTTACATGATGCTCTCTGAGGCGAGAGAGACACATGAACTGTGTGG 1260  
QY 1352 GACACACAGAACTATGATGCGCGACAGAAAGTTTGGGTTCTGCCCATGGCTGCCCAAGA 1411  
Db 1261 GACACACAGAACTATGATGCGCGACAGAAAGTTTGGGTTCTGCCCATGGCTGCCCAAGA 1320  
QY 1412 GGAATCTGCAACAACAATGAAGGGTCTATGACCGCATTTGAGATGAGATGAGTGAAGCA 1471  
Db 1321 GGAATCTGCAACAACAATGAAGGGTCTATGACCGCATTTGAGATGAGATGAGTGAAGCA 1380  
QY 1472 GCATGACATGGGTCTACATGATGAGTGCACGTGTGTTGGGAATGCTCGTGGGGAATGGAC 1531  
Db 1381 GCATGACATGGGTCTACATGATGAGTGCACGTGTGTTGGGAATGCTCGTGGGGAATGGAC 1440  
QY 1532 ATGCATTGCTTACTCGCAGCTTCGAGATCAGTGCATTTGTTGATGACATCACTTACAATGT 1591  
Db 1441 ATGCATTGCTTACTCGCAGCTTCGAGATCAGTGCATTTGTTGATGACATCACTTACAATGT 1500  
QY 1592 GAAACGACATTTCCAAAGCGTCATGAAGAGGGGCAATGCTGAACTGATCATGCTTGG 1651  
Db 1501 GAAACGACATTTCCAAAGCGTCATGAAGAGGGGCAATGCTGAACTGATCATGCTTGG 1560  
QY 1652 TCAGGTCGGGCGAGTGAAGTGTGATCCCGTCGACCAATGCCAGGATTCAGAGACTGG 1711  
Db 1561 TCAGGTCGGGCGAGTGAAGTGTGATCCCGTCGACCAATGCCAGGATTCAGAGACTGG 1620  
QY 1712 GACGTTTATCAAAATGGAGATTCATGGGAGAGTATGTGCAATGTTGATGATACCAATGT 1771  
Db 1621 GACGTTTATCAAAATGGAGATTCATGGGAGAGTATGTGCAATGTTGATGATACCAATGT 1680  
QY 1772 CTACTGCTATGCGCGTGGGAGTGGGAGTGGGCAATGCGCAATCTTTACAGACTTCCAAAG 1831  
Db 1681 CTACTGCTATGCGCGTGGGAGTGGGAGTGGGCAATGCGCAATCTTTACAGACTTCCAAAG 1740  
QY 1832 CTCAGTGTCTGTCGAGTATTTATCACTGAGCTCCGAGTCCGAGTCCCACTCCCAACC 1891  
Db 1741 CTCAGTGTCTGTCGAGTATTTATCACTGAGCTCCGAGTCCGAGTCCCACTCCCAACC 1800  
QY 1892 CATCCAGTGGAAATGCAACCAAGCATCTCACATTTCCAAAGTACATTTCTCAGGTGGAGACC 1951  
Db 1801 CATCCAGTGGAAATGCAACCAAGCATCTCACATTTCCAAAGTACATTTCTCAGGTGGAGACC 1860  
QY 1952 T 1952  
Db 1861 T 1861

RESULT 5  
US-09-023-655-1289  
; Sequence 1289, Application US/09023655  
; Patent No. 6607879  
; GENERAL INFORMATION:  
; APPLICANT: Cocks, Benjamin G.  
; APPLICANT: Susan G. Stuart  
; APPLICANT: Jeffrey J. Seilhamer  
; TITLE OF INVENTION: COMPOSITION FOR THE DETECTION OF BLOOD CELL GENE  
; TITLE OF INVENTION: EXPRESSION  
; NUMBER OF SEQUENCES: 1508  
; CORRESPONDENCE ADDRESS:  
; ADDRESSEE: INCYTE PHARMACEUTICALS, INC.  
; STREET: 3174 PORTER DRIVE  
; CITY: PALO ALTO  
; STATE: CALIFORNIA  
; COUNTRY: USA  
; ZIP: 94304  
; COMPUTER READABLE FORM:  
; MEDIUM TYPE: Floppy disk  
; COMPUTER: IBM PC compatible  
; OPERATING SYSTEM: PC-DOS/MS-DOS

SOFTWARE: Word Perfect 6.1 for Windows/MS-DOS 6.2  
CURRENT APPLICATION DATA:  
APPLICATION NUMBER: US/09/023,655  
FILING DATE: HERewith  
CLASSIFICATION:  
PRIOR APPLICATION DATA:  
APPLICATION NUMBER:  
FILING DATE:  
CLASSIFICATION:  
ATTORNEY/AGENT INFORMATION:  
NAME: Zeller, Karen J.  
REGISTRATION NUMBER: 37,071  
REFERENCE/DOCKET NUMBER: PA-0001 US  
TELECOMMUNICATION INFORMATION:  
TELEPHONE: (650) 855-0555  
TELEFAX: (650) 845-4166  
INFORMATION FOR SEQ ID NO: 1289:  
SEQUENCE CHARACTERISTICS:  
LENGTH: 7680 base pairs  
TYPE: nucleic acid  
STRANDEDNESS: single  
TOPOLOGY: linear  
IMMEDIATE SOURCE:  
LIBRARY: GENBANK  
CLONE: g31396  
US-09-023-655-1289

Query Match 81.2%; Score 1743.4; DB 4; Length 7680;  
Best Local Similarity 97.0%; Pred. No. 0;  
Matches 1805; Conservative 0; Mismatches 11; Indels 45; Gaps 1;  
QY 137 GAAGAGCAAGAGGAGGAGGCTCAGCAAAATGGTTTCAGCCCCAGCTCCCGGTGGCTGTGAGTCA 196  
Db 1 GAAGAGCAAGAGGAGGAGGCTCAGCAAAATGGTTTCAGCCCCAGCTCCCGGTGGCTGTGAGTCA 60  
QY 197 AAGCAAGCCCGGTTGTTATGACAATGGAAGAACATATCAGATAAATCAACAGTGGAGCG 256  
Db 61 AAGCAAGCCCGGTTGTTATGACAATGGAAGAACATATCAGATAAATCAACAGTGGAGCG 120  
QY 257 GACCTACCTAGGCATGCTGGTTGTTGTTTATGAGGAGAACCGAGGTTTAACTG 316  
Db 121 GACCTACCTAGGTAATGTTGTTGTTTATGAGGAGAACCGAGGTTTAACTG 180  
QY 317 CGAGAGTAAACCTGAAGCTGAAGAGACTTGTCTTTCAGCAAGTACACTTGGGAACTTACCG 376  
Db 181 CGAAAGTAAACCTGAAGCTGAAGAGACTTGTCTTTCAGCAAGTACACTTGGGAACTTACCG 240  
QY 377 AGTGGGTGACACTTATGAGCGTCTTAAAGACTTCCATGATCTGGGACTGTGACCTGCATCGG 436  
Db 241 AGTGGGTGACACTTATGAGCGTCTTAAAGACTTCCATGATCTGGGACTGTGACCTGCATCGG 300  
QY 437 GGCTGGGCGAGGAGCAATTAAGCTGTACCATCGCAACCGCTGCCATGAAGGGGTGAGTTC 496  
Db 301 GGCTGGGCGAGGAGCAATTAAGCTGTACCATCGCAACCGCTGCCATGAAGGGGTGAGTTC 360  
QY 497 CTACAAGATTGTTGACACCTCGAGGAGAGCAATGAGACTGTGTGTTTACATGTTAGAGTG 556  
Db 361 CTACAAGATTGTTGACACCTCGAGGAGAGCAATGAGACTGTGTGTTTACATGTTAGAGTG 420  
QY 557 TGTGTGTTGTTGTAATGGAAGAGAGTGAACCTTGAAGCCCATAGCTGAGAGTGTGTTT 616  
Db 421 TGTGTGTTGTTGTAATGGAAGAGAGTGAACCTTGAAGCCCATAGCTGAGAGTGTGTTT 480  
QY 617 TGATCATGCTGCTGGGACTTCTCTATGTTGTCGAGAGAACGTCGGAGAACCCCTACCAAGG 676  
Db 481 TGATCATGCTGCTGGGACTTCTCTATGTTGTCGAGAGAACGTCGGAGAACCCCTACCAAGG 540  
QY 677 CTGGATGATGTTAGATTGTACTTGTGCTGGGAGAGGAGCGGAGCGCATCACTTGCATTC 736  
Db 541 CTGGATGATGTTAGATTGTACTTGTGCTGGGAGAGGAGCGGAGCGCATCACTTGCATTC 600  
QY 737 TAGAAATAGATGCAACGATCAGAGACAAAGGACATCTTATAGAAATTTGGAGACACCTGGAG 796